

# WEST Search History

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DATE: Monday, November 14, 2005

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<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L30	L28 and prostate	2
<input type="checkbox"/>	L29	L28 and melanoma	2
<input type="checkbox"/>	L28	20020039754	2
<input type="checkbox"/>	L27	Fruehauf-john.in.	5
<input type="checkbox"/>	L26	taylor-clive-r.in.	14
<input type="checkbox"/>	L25	skinner-donald-g.in.	0
<input type="checkbox"/>	L24	groshen-susan.in.	0
<input type="checkbox"/>	L23	esrig-david.in.	0
<input type="checkbox"/>	L22	bochner-bernard-h.in.	0
<input type="checkbox"/>	L21	stein-john-p.in.	7
<input type="checkbox"/>	L20	ginsberg-david-a.in.	0
<input type="checkbox"/>	L19	grossfeld-gary-d.in.	0
<input type="checkbox"/>	L18	cote-richard-j.in.	6
<input type="checkbox"/>	L17	cote-r.in.	30
<input type="checkbox"/>	L16	Bouck-noel-p.in.	15
<input type="checkbox"/>	L15	L14 and l10	316
<input type="checkbox"/>	L14	L13 and l11	330
<input type="checkbox"/>	L13	p53	157705
<input type="checkbox"/>	L12	Lp53	10
<input type="checkbox"/>	L11	TSP-1	515
<input type="checkbox"/>	L10	angiogenesis	26625
<input type="checkbox"/>	L9	L8 and angiogenesis	318
<input type="checkbox"/>	L8	L7 and l3	342
<input type="checkbox"/>	L7	thrombospondin-1	659
<input type="checkbox"/>	L6	bouck-n.in.	0
<input type="checkbox"/>	L5	Dameron-k.in.	0
<input type="checkbox"/>	L4	L2 and l3	57
<input type="checkbox"/>	L3	p53	157705
<input type="checkbox"/>	L2	brawer	208
<input type="checkbox"/>	L1	brawer-mk.in.	0

END OF SEARCH HISTORY

## Refine Search

### Search Results -

Terms	Documents
10734880	0

**Database:**

US Pre-Grant Publication Full-Text Database  
US Patents Full-Text Database  
US OCR Full-Text Database  
EPO Abstracts Database  
JPO Abstracts Database  
Derwent World Patents Index  
IBM Technical Disclosure Bulletins

**Search:**

L6

Refine Search

Recall Text Clear Interrupt

### Search History

**DATE: Monday, November 14, 2005** [Printable Copy](#) [Create Case](#)

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES;			
OP=ADJ			
<u>L6</u>	10734880	0	<u>L6</u>
<u>L5</u>	10295188	3	<u>L5</u>
<u>L4</u>	10144142	4	<u>L4</u>
<u>L3</u>	fruehauf-john.in.	5	<u>L3</u>
<u>L2</u>	5840507.pn.	2	<u>L2</u>
<u>L1</u>	6303324.pn.	2	<u>L1</u>

END OF SEARCH HISTORY

# Freeform Search

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<b>Database:</b>	US Pre-Grant Publication Full-Text Database US Patents Full-Text Database US OCR Full-Text Database EPO Abstracts Database JPO Abstracts Database Derwent World Patents Index IBM Technical Disclosure Bulletins
<b>Term:</b>	<input type="text" value="L8 and angiogenesis"/> <div style="position: absolute; right: -10px; top: 0px; width: 10px; height: 10px; background-color: black; border: none;"></div> <div style="position: absolute; right: -10px; bottom: -5px; width: 10px; height: 10px; background-color: black; border: none;"></div>
<b>Display:</b>	10 <input type="text"/> Documents in <u>Display Format:</u> <input type="text"/> Starting with Number <input type="text"/> 1 <input type="radio"/>
<b>Generate:</b>	<input type="radio"/> Hit List <input type="radio"/> Hit Count <input type="radio"/> Side by Side <input type="radio"/> Image

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## Search History

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**DATE:** Monday, November 14, 2005 [Printable Copy](#) [Create Case](#)

<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
side by side			result set
<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES;</i>			
<i>OP=ADJ</i>			
<u>L9</u>	L8 and angiogenesis	318	<u>L9</u>
<u>L8</u>	L7 and l3	342	<u>L8</u>
<u>L7</u>	thrombospondin-1	659	<u>L7</u>
<u>L6</u>	bouck-n.in.	0	<u>L6</u>
<u>L5</u>	Dameron-k.in.	0	<u>L5</u>
<u>L4</u>	L2 and l3	57	<u>L4</u>
<u>L3</u>	p53	157705	<u>L3</u>
<u>L2</u>	brawer	208	<u>L2</u>
<u>L1</u>	brawer-mk.in.	0	<u>L1</u>

END OF SEARCH HISTORY

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of CAplus documents for use in third-party analysis and  
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NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT  
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
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FILE 'HOME' ENTERED AT 14:05:42 ON 14 NOV 2005

=> FIL MEDLINE, BIOSIS, EMBASE  
COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE ENTRY	TOTAL SESSION
0.21	0.21

FILE 'MEDLINE' ENTERED AT 14:05:55 ON 14 NOV 2005

FILE 'BIOSIS' ENTERED AT 14:05:55 ON 14 NOV 2005  
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FILE 'EMBASE' ENTERED AT 14:05:55 ON 14 NOV 2005  
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=> s p53  
L1 114062 P53

=> s thrombospondin-1  
L2 3207 THROMBOSPONDIN-1

=> s angiogenesis  
L3 81008 ANGIOGENESIS

=> s l1 and l2  
L4 244 L1 AND L2

=> s l3 and l4  
L5 183 L3 AND L4

=> duplicate remove  
ENTER L# LIST OR (END):15  
DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS, EMBASE'  
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n  
PROCESSING COMPLETED FOR L5  
L6 106 DUPLICATE REMOVE L5 (77 DUPLICATES REMOVED)

=> s breast cancer  
L7 291994 BREAST CANCER

=> l6 and l7  
L6 IS NOT A RECOGNIZED COMMAND  
The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> s l6 and l7  
L8 14 L6 AND L7

=> s prostate cancer  
L9 103114 PROSTATE CANCER

=> s l6 and l9  
L10 6 L6 AND L9

=> s melanoma  
L11 170286 MELANOMA

=> s l6 and l11  
L12 9 L6 AND L11

=> s l8 or l10  
L13 18 L8 OR L10

=> s l13 or l12  
L14 26 L13 OR L12

=> display l14  
ENTER ANSWER NUMBER OR RANGE (1):1-26  
ENTER DISPLAY FORMAT (FILEDEFAULT):all

L14 ANSWER 1 OF 26 MEDLINE on STN  
AN 2002182450 MEDLINE  
DN PubMed ID: 11916242  
TI Aerosol delivery of PEI-p53 complexes inhibits B16-F10 lung metastases through regulation of angiogenesis.  
AU Gautam Ajay; Densmore Charles L; Melton Sara; Golunski Eva; Waldrep J Clifford  
CS Department of Molecular Physiology and Biophysics, Baylor College of Medicine, Houston, Texas 77030, USA.  
SO Cancer gene therapy, (2002 Jan) 9 (1) 28-36.  
Journal code: 9432230. ISSN: 0929-1903.  
CY England: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200207  
ED Entered STN: 20020403  
Last Updated on STN: 20020710  
Entered Medline: 20020709  
AB Inhibition of pulmonary metastases poses a difficult clinical challenge for current therapeutic regimens. We have developed an aerosol system utilizing a cationic polymer, polyethyleneimine (PEI), for topical gene delivery to the lungs as a novel approach for treatment of lung cancer. Using a B16-F10 murine melanoma model in C57BL/6 mice, we previously demonstrated that aerosol delivery of PEI-p53 DNA resulted in highly significant reductions in the tumor burden ( $P < .001$ ) in treated animals, and also lead to about 50% increase in the mean length of survival of the mice-bearing B16-F10 lung tumors. The mechanisms of this antitumor effect of p53 are investigated in this report. Here, we demonstrate that the p53 transfection leads to an up-regulation of the antiangiogenic factor thrombospondin-1 (TSP-1) in the lung tissue and the serum of the mice. Furthermore, there is a down-regulation of vascular endothelial growth factor (VEGF) in the lung tissue and serum of the B16-F10 tumor-bearing mice treated with PEI-p53 DNA complexes, compared with untreated tumor-bearing animals. In addition, staining for von Willebrand factor (vWF), a marker for the angiogenic blood vessels, revealed that p53 treatment leads to a decrease in the angiogenic phenotype of the B16-F10 tumors. Immunohistochemistry for transgene expression reveals that the PEI-p53 aerosol complexes transfect mainly the epithelial cells lining the airways, with diffuse transfection in the alveolar lining cells, as well as, the tumor foci in the lung tissue. There was also some evidence of apoptosis in the lung tumor foci of animals treated with p53. The data suggest that aerosol delivery of PEI-p53 complexes leads to inhibition of B16-F10 lung metastases, in part by suppression of angiogenesis.  
CT Check Tags: Female  
Administration, Inhalation  
Animals  
Chloramphenicol O-Acetyltransferase: ME, metabolism  
DNA: AD, administration & dosage  
\*Drug Delivery Systems  
Endothelial Growth Factors: ME, metabolism  
\*Gene Therapy: MT, methods  
\*Genes, p53: GE, genetics  
Genetic Vectors  
Humans  
Lung Neoplasms: BS, blood supply  
\*Lung Neoplasms: PC, prevention & control  
Lung Neoplasms: SC, secondary  
Lymphokines: ME, metabolism  
Melanoma, Experimental: BS, blood supply  
Melanoma, Experimental: PA, pathology  
\*Melanoma, Experimental: PC, prevention & control

Mice  
Mice, Inbred C57BL  
\*Neovascularization, Pathologic: ME, metabolism  
Polyethyleneimine: AD, administration & dosage  
Thrombospondin 1: ME, metabolism  
Transfection  
Up-Regulation: PH, physiology  
Vascular Endothelial Growth Factor A  
Vascular Endothelial Growth Factors  
RN 9002-98-6 (Polyethyleneimine); 9007-49-2 (DNA)  
CN 0 (Endothelial Growth Factors); 0 (Genetic Vectors); 0 (Lymphokines); 0 (Thrombospondin 1); 0 (Vascular Endothelial Growth Factor A); 0 (Vascular Endothelial Growth Factors); EC 2.3.1.28 (Chloramphenicol O-Acetyltransferase)

L14 ANSWER 2 OF 26 MEDLINE on STN  
AN 2002121277 MEDLINE  
DN PubMed ID: 11856116  
TI Thrombospondin-1, vascular endothelial growth factor expression and their relationship with p53 status in prostate cancer and benign prostatic hyperplasia.  
AU Kwak C; Jin R J; Lee C; Park M S; Lee S E  
CS Department of Urology and Clinical Research Institute, Seoul National University College of Medicine, Seoul, Korea.  
SO BJU international, (2002 Feb) 89 (3) 303-9.  
Journal code: 100886721. ISSN: 1464-4096.  
CY England: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200203  
ED Entered STN: 20020222  
Last Updated on STN: 20020324  
Entered Medline: 20020322  
AB OBJECTIVE: To evaluate the expression of thrombospondin-1 (TSP-1, a potent inhibitor of angiogenesis) and vascular endothelial growth factor (VEGF, an important angiogenic factor in solid tumours) in prostate cancer, and their relationship with p53 status. PATIENTS AND METHODS: Using immunohistochemistry, the expression of VEGF, TSP-1 and p53 was assessed in 82 archival tissue specimens from 23 patients with benign prostatic hyperplasia (BPH), 22 with localized prostate cancer and 37 with metastatic prostate cancer. Seven of the last group had received androgen deprivation therapy. The relationship between the expression of VEGF, TSP-1 and p53 status was also evaluated with tumour grade and stage in patients with prostate cancer. RESULTS: The seven patients receiving hormonal treatment were excluded from the analysis because androgen deprivation significantly increased TSP-1 and decreased VEGF expression (both P < 0.01). Immunohistochemical analysis showed significantly higher VEGF and significantly lower TSP-1 expression (both P < 0.01) in prostate cancer than in BPH tissues. There was also significantly higher VEGF and significantly lower TSP-1 expression (both P < 0.05) in tissues from metastatic than localized prostate cancer. There was no significant correlation between VEGF or TSP-1 expression and Gleason score, but a significant inverse correlation between TSP-1 and VEGF expression. There was a significant association between VEGF expression and p53 status (P < 0.05), but TSP-1 expression was not associated with p53 status. CONCLUSIONS: Angiogenic factors, including VEGF and TSP-1, might be important in the development and progression of prostate cancer. These changes seem to be influenced by p53 status. Identifying the angiogenic factors involved in prostate cancer might lead to the development of diagnostic or therapeutic strategies based on

CT anti-angiogenesis.  
Check Tags: Male  
Adenocarcinoma: BS, blood supply  
\*Adenocarcinoma: ME, metabolism  
Aged  
Aged, 80 and over  
Disease Progression  
\*Endothelial Growth Factors: ME, metabolism  
Humans  
Immunohistochemistry  
\*Lymphokines: ME, metabolism  
Middle Aged  
Neovascularization, Pathologic  
\*Prostatic Hyperplasia: ME, metabolism  
Prostatic Neoplasms: BS, blood supply  
\*Prostatic Neoplasms: ME, metabolism  
\*Protein p53: ME, metabolism  
Research Support, Non-U.S. Gov't  
\*Thrombospondin 1: ME, metabolism  
Vascular Endothelial Growth Factor A  
Vascular Endothelial Growth Factors  
CN 0 (Endothelial Growth Factors); 0 (Lymphokines); 0 (Protein p53)  
); 0 (Thrombospondin 1); 0 (Vascular Endothelial  
Growth Factor A); 0 (Vascular Endothelial Growth Factors)

L14 ANSWER 3 OF 26 MEDLINE on STN  
AN 2002071060 MEDLINE  
DN PubMed ID: 11796289  
TI Thrombospondin-1 expression in patients with  
pathologic stage T3 prostate cancer undergoing radical  
prostatectomy: association with p53 alterations, tumor  
angiogenesis, and tumor progression.  
AU Grossfeld Gary D; Carroll Peter R; Lindeman Neil; Meng Maxwell; Groshen  
Susan; Feng An Chen; Hawes Debra; Cote Richard J  
CS Department of Urology, University of California, San Francisco, School of  
Medicine, San Francisco, California 94115-1711, USA.  
SO Urology, (2002 Jan) 59 (1) 97-102.  
Journal code: 0366151. ISSN: 1527-9995.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200202  
ED Entered STN: 20020125  
Last Updated on STN: 20020213  
Entered Medline: 20020212  
AB OBJECTIVES: To investigate thrombospondin-1 (TSP)  
expression in patients with prostate cancer undergoing  
radical prostatectomy. TSP is a p53-dependent inhibitor of  
tumor angiogenesis. Previous studies have demonstrated that TSP  
expression is significantly associated with the microvessel density (MVD)  
count, p53 expression, and disease-specific and overall survival  
in patients with invasive bladder cancer undergoing radical cystectomy.  
METHODS: Radical prostatectomy specimens from 85 patients with pathologic  
Stage T3 disease were analyzed for TSP expression, p53 nuclear  
reactivity, and MVD using antigen-retrieval immunohistochemistry. The  
median follow-up after surgery was 10.6 years (range 1.8 to 15.4).  
Disease recurrence was defined as a prostate-specific antigen level of 0.2  
ng/mL or greater on two consecutive occasions after surgery. TSP  
expression was graded as present or absent on the basis of the  
immunoreactivity in the extracellular matrix by persons unaware of the  
clinical outcome. Specimens were considered p53 positive  
(altered) if more than 10% of the tumor cells demonstrated nuclear  
reactivity. The chi-square test was used to determine whether the

associations were significant between the pathologic tumor characteristics and the immunohistochemical findings. The log-rank test was used to determine the associations between the immunohistochemical findings and disease recurrence. RESULTS: TSP and p53 were graded as positive in 21 (26%) and 16 (19%) tumors, respectively. The median MVD count was 111.5. No significant associations were found among p53 status, TSP expression, and MVD. Seminal vesicle invasion and Gleason pattern 4 or 5 disease were significant predictors of disease recurrence. A trend was noted toward a higher rate of disease recurrence for patients with altered p53 expression (p53 positive) or increased MVD. TSP expression was not associated with disease recurrence. CONCLUSIONS: We found no significant association between TSP expression and p53 status, MVD count, or outcome after radical prostatectomy for patients with pathologic Stage T3 prostate cancer. Our data suggest that p53 and MVD may be associated with outcome in these patients. Additional studies are needed to identify reliable molecular markers of outcome for patients with this disease.

CT Check Tags: Male  
\*Adenocarcinoma: CH, chemistry  
Adenocarcinoma: PA, pathology  
Adenocarcinoma: SU, surgery  
Follow-Up Studies  
Humans  
Middle Aged  
Neoplasm Recurrence, Local: BL, blood  
Neoplasm Recurrence, Local: DI, diagnosis  
Neoplasm Staging  
Prostate-Specific Antigen: BL, blood  
Prostatectomy  
\*Prostatic Neoplasms: CH, chemistry  
Prostatic Neoplasms: PA, pathology  
Prostatic Neoplasms: SU, surgery  
\*Protein p53: AN, analysis  
\*Thrombospondin 1: AN, analysis  
\*Tumor Markers, Biological: AN, analysis  
CN 0 (Protein p53); 0 (Thrombospondin 1); 0  
(Tumor Markers, Biological); EC 3.4.21.77 (Prostate-Specific Antigen)

L14 ANSWER 4 OF 26 MEDLINE on STN  
AN 2001155324 MEDLINE  
DN PubMed ID: 11205922  
TI Independent association of angiogenesis index with outcome in prostate cancer.  
AU Mehta R; Kyshtoobayeva A; Kurosaki T; Small E J; Kim H; Stroup R; McLaren C E; Li K T; Fruehauf J P  
CS Oncotech Incorporated, Irvine, California 92614, USA.  
SO Clinical cancer research : an official journal of the American Association for Cancer Research, (2001 Jan) 7 (1) 81-8.  
Journal code: 9502500. ISSN: 1078-0432.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200103  
ED Entered STN: 20010404  
Last Updated on STN: 20010404  
Entered Medline: 20010322  
AB New molecular factors have been characterized that are associated with the prognosis of prostate carcinoma patients, including p53 status and angiogenesis. We reported recently that mutant p53 (mp53) was associated with decreased expression of an endogenous inhibitor of angiogenesis, thrombospondin-1 (TSP-1), and increased microvessel density in melanoma and breast

cancer. In this study, we performed a similar analysis on primary prostate carcinoma to determine whether these factors were associated with each other or patient outcomes. Paraffin-embedded specimens of 98 cases of primary prostate carcinoma were obtained and examined to confirm tissue diagnosis and Gleason scores. Carcinoma-specific levels of p53, TSP-1, and tumor angiogenesis were determined using semiquantitative immunohistochemistry (IHC) methods. Acquisition of mp53 was significantly associated with decreased TSP-1 ( $P = 0.002$ ) and increased angiogenesis ( $P < 0.0001$ ). An angiogenesis index integrating mp53, TSP-1, and angiogenesis (CD31) scores was found to be an independent predictor of survival in univariate and multivariate analyses that included Gleason score, clinical stage, and patient age. Further validation of the angiogenesis index in prostate carcinoma may provide a new tool to stratify patient risk.

CT Check Tags: Male

\*Adenocarcinoma: BS, blood supply

Adenocarcinoma: ME, metabolism

Adenocarcinoma: SU, surgery

Aged

Antigens, CD31: ME, metabolism

Biopsy, Needle

Disease Progression

Humans

Image Processing, Computer-Assisted

Immunoenzyme Techniques

Mutation

Neovascularization, Pathologic: ME, metabolism

\*Neovascularization, Pathologic: PA, pathology

Neovascularization, Pathologic: SU, surgery

Paraffin Embedding

Prostatectomy

\*Prostatic Neoplasms: BS, blood supply

Prostatic Neoplasms: ME, metabolism

Prostatic Neoplasms: SU, surgery

    Protein p53: ME, metabolism

Retrospective Studies

Survival Analysis

    Thrombospondin 1: ME, metabolism

Tumor Markers, Biological: ME, metabolism

CN 0 (Antigens, CD31); 0 (Protein p53); 0 (Thrombospondin 1); 0 (Tumor Markers, Biological)

L14 ANSWER 5 OF 26 MEDLINE on STN

AN 2001118033 MEDLINE

DN PubMed ID: 11150912

TI Thrombospondin-1 and -2 in node-negative breast cancer: correlation with angiogenic factors, p53, cathepsin D, hormone receptors and prognosis.

AU Gasparini G; Toi M; Biganzoli E; Dittadi R; Fanelli M; Morabito A; Boracchi P; Gion M

CS Division of Medical Oncology, Azienda Complesso Ospedaliero 'San Filippo Neri', Rome, Italy.

SO Oncology, (2001) 60 (1) 72-80.

Journal code: 0135054. ISSN: 0030-2414.

CY Switzerland

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200102

ED Entered STN: 20010322

Last Updated on STN: 20010322

Entered Medline: 20010215

AB OBJECTIVE: Thrombospondins (TSP(s)) are a multigene family of five secreted glycoproteins involved in the regulation of cell proliferation,

adhesion and migration. Two members of the TSP family, namely TSP-1 and TSP-2, are also naturally occurring inhibitors of angiogenesis. The aim of the present study was to determine the prognostic significance of the determination of TSP-1 and -2 and their correlation with the angiogenic peptides vascular endothelial growth factor (VEGF) and thymidine phosphorylase (TP), as well as with other biological and clinicopathological features investigated. METHODS: We evaluated a series of 168 women with node-negative breast cancer with a median follow-up period of 66 months, not treated with adjuvant therapy. The cytosolic levels of TSP-1 and -2 were determined in the primary tumour by a commercially available immunometric assay. RESULTS: We found that 166 tested tumours had measurable levels of TSP-1 and -2 protein (median value 5.978, range 0.579-31.410 ng/mg of protein). On the basis of Spearman's rank correlation coefficient, a weak inverse association of TSP-1 and -2 with tumour size and cathepsin D was found. Moreover, principal component analysis on ranks evidenced a poor association between TSP-1 and -2, VEGF and TP. The results of the clinical outcome were analysed by both univariate and multivariate [for relapse-free survival (RFS) only] Cox regression models. TSP-1 and -2 were not significant prognostic factors in univariate analysis for either RFS ( $p = 0.427$ ) or overall survival ( $p = 0.069$ ). To investigate the 'angiogenic balance hypothesis', bivariate analyses were performed to investigate the interactions of TSP-1 and -2 with VEGF, TP or p53, but none were included in the selected models. Finally, in multivariate analysis for RFS a baseline model, previously defined in a larger case series and inclusive of VEGF, TP and their interaction was adopted. It was highly significant ( $p = 0.002$ , Harrell c statistic value of 0.703); but when TSP-1 and -2 were added, their contribution was negligible ( $p = 0.731$ , Harrell c statistic value of 0.705). CONCLUSIONS: The results of this study suggest that TSP-1 and -2 do not provide additional prognostic contribution to the joint effects of VEGF and TP. In the series of node-negative breast cancer patients investigated, determination of the angiogenic peptides VEGF and TP gave significant prognostic information. On the contrary, TSP-1 and -2, potential naturally occurring negative regulators of angiogenesis, lacked prognostic value.

CT

Check Tags: Female  
\*Breast Neoplasms: CH, chemistry  
Breast Neoplasms: PA, pathology  
\*Cathepsin D: AN, analysis  
Cytosol: CH, chemistry  
\*Endothelial Growth Factors: AN, analysis  
Humans  
Immunohistochemistry  
\*Lymphokines: AN, analysis  
Neovascularization, Pathologic: ME, metabolism  
Predictive Value of Tests  
Prognosis  
Proportional Hazards Models  
\*Protein p53: AN, analysis  
\*Receptors, Estrogen: AN, analysis  
\*Receptors, Progesterone: AN, analysis  
Research Support, Non-U.S. Gov't  
Thrombospondin 1: AN, analysis  
\*Thrombospondins: AN, analysis  
Thymidine Phosphorylase: AN, analysis  
\*Tumor Markers, Biological: AN, analysis  
Vascular Endothelial Growth Factor A  
Vascular Endothelial Growth Factors

CN

0 (Endothelial Growth Factors); 0 (Lymphokines); 0 (Protein p53); 0 (Receptors, Estrogen); 0 (Receptors, Progesterone); 0 (Thrombospondin 1); 0 (Thrombospondins); 0 (Tumor Markers, Biological); 0 (Vascular Endothelial Growth Factor A); 0 (Vascular Endothelial Growth Factors); EC 2.4.2.4 (Thymidine

Phosphorylase); EC 3.4.23.5 (Cathepsin D)

L14 ANSWER 6 OF 26 MEDLINE on STN  
AN 2000182650 MEDLINE  
DN PubMed ID: 10719731  
TI p53 and vascular-endothelial-growth-factor (VEGF) expression predicts outcome in 833 patients with primary breast carcinoma.  
AU Linderholm B; Lindh B; Tavelin B; Grankvist K; Henriksson R  
CS Department of Oncology, Umea University, Sweden..  
Barbro.Linderholm@onkologi.umu.se  
SO International journal of cancer. Journal international du cancer, (2000 Jan 20) 89 (1) 51-62.  
Journal code: 0042124. ISSN: 0020-7136.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200003  
ED Entered STN: 20000330  
Last Updated on STN: 20000330  
Entered Medline: 20000321  
AB The angiogenic factor vascular endothelial growth factor (VEGF) predicts outcome in primary breast carcinoma. Alteration of the p53 gene causes down-regulation of the expression of *thrombospondin-1*, a natural inhibitor of angiogenesis. This study was conducted to investigate the association between mutant p53 protein and VEGF expression, and the prognostic value of these factors. VEGF165 and p53 protein were measured in tumour cytosols by enzyme immunoassays. Recurrence-free survival (RFS) and overall survival (OS) were estimated in 833 consecutive patients, 485 node-negative (NNBC) and 348 node-positive (NPBC) with primary invasive breast cancer. A significant association was found between mutant p53 protein and VEGF expression. Univariate analysis showed both p53 and VEGF to be significant predictors of survival. Similar correlation was seen when p53 was combined with VEGF. Univariate analysis of NNBC showed significant prognostic value of p53 for OS, also when combined with VEGF expression; for NPBC, significant reductions in RFS and OS were seen for p53-positive patients, and these findings were enhanced when combined with VEGF, also in the sub-group receiving adjuvant endocrine treatment. Multivariate analysis showed both p53 and VEGF as independent predictors of OS in all groups. When the 2 factors were combined, an increased relative risk of 2.7 was seen for OS in the group with both p53 positivity and high VEGF content, as compared with 1.7 in the group with one risk factor. The results suggest an association between loss of wt-p53 and increased VEGF expression, indicating that angiogenic activity may depend, at least partly, on altered p53-protein function. Combination of these 2 biological markers appears to give additional predictive information of survival. A high-risk group of patients was associated with p53 positivity and higher VEGF content.  
CT Check Tags: Female  
Breast Neoplasms: BS, blood supply  
\*Breast Neoplasms: ME, metabolism  
Breast Neoplasms: MO, mortality  
Breast Neoplasms: PA, pathology  
\*Endothelial Growth Factors: ME, metabolism  
Humans  
\*Lymphokines: ME, metabolism  
Multivariate Analysis  
Neovascularization, Pathologic  
Prognosis  
Proportional Hazards Models  
\*Protein p53: ME, metabolism

Receptors, Estrogen: ME, metabolism  
Receptors, Progesterone: ME, metabolism  
Research Support, Non-U.S. Gov't  
Survival Analysis  
Vascular Endothelial Growth Factor A  
Vascular Endothelial Growth Factors

CN 0 (Endothelial Growth Factors); 0 (Lymphokines); 0 (Protein p53); 0 (Receptors, Estrogen); 0 (Receptors, Progesterone); 0 (Vascular Endothelial Growth Factor A); 0 (Vascular Endothelial Growth Factors); 0 (vascular endothelial growth factor A, human)

L14 ANSWER 7 OF 26 MEDLINE on STN  
AN 1999240722 MEDLINE  
DN PubMed ID: 10224095  
TI Systemic gene delivery expands the repertoire of effective antiangiogenic agents.  
AU Liu Y; Thor A; Shtivelman E; Cao Y; Tu G; Heath T D; Debs R J  
CS Geraldine Brush Cancer Research Institute at the California Pacific Medical Center, San Francisco, California 94115, USA.  
NC CA58207 (NCI)  
CA58914 (NCI)  
CA71422 (NCI)  
SO Journal of biological chemistry, (1999 May 7) 274 (19) 13338-44.  
Journal code: 2985121R. ISSN: 0021-9258.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199906  
ED Entered STN: 19990614  
Last Updated on STN: 19990614  
Entered Medline: 19990603  
AB Cationic liposome-DNA complex (CLDC)-based intravenous gene delivery targets gene expression to vascular endothelial cells, macrophages and tumor cells. We used systemic gene delivery to identify anti-angiogenic gene products effective against metastatic spread in tumor-bearing mice. Specifically, CLDC-based intravenous delivery of the p53 and GM-CSF genes were each as effective as the potent antiangiogenic gene, angiostatin, in reducing both tumor metastasis and tumor angiogenesis. Combined delivery of these genes did not increase anti-tumor activity, further suggesting that each gene appeared to produce its antimetastatic activity through a common antiangiogenic pathway. CLDC-based intravenous delivery of the human wild type p53 gene transfected up to 80% of tumor cells metastatic to lung. Furthermore, it specifically induced the expression of the potent antiangiogenic gene, thrombospondin-1, indicating that p53 gene delivery in vivo may inhibit angiogenesis by inducing endogenous thrombospondin-1 expression. CLDC-based delivery also identified a novel anti-tumor activity for the metastasis suppressor gene CC3. Thus, CLDC-based intravenous gene delivery can produce systemic antiangiogenic gene therapy using a variety of different genes and may be used to assess potential synergy of combined anti-tumor gene delivery and to identify novel activities for existing anti-tumor genes.  
CT Angiostatins  
Animals  
Gene Expression  
\*Gene Transfer Techniques  
    Genes, p53: GE, genetics  
Granulocyte-Macrophage Colony-Stimulating Factor: GE, genetics  
Humans  
    \*Melanoma, Experimental: BS, blood supply  
    Melanoma, Experimental: GE, genetics  
    Melanoma, Experimental: PA, pathology  
Mice

\*Neoplasm Metastasis: TH, therapy  
    Neovascularization, Pathologic: GE, genetics  
\*Neovascularization, Pathologic: TH, therapy  
    Peptide Fragments: GE, genetics  
    Plasminogen: GE, genetics  
    Research Support, Non-U.S. Gov't  
    Research Support, U.S. Gov't, P.H.S.  
        Thrombospondin 1: GE, genetics

RN 83869-56-1 (Granulocyte-Macrophage Colony-Stimulating Factor); 86090-08-6  
    (Angiostatins); 9001-91-6 (Plasminogen)

CN 0 (Peptide Fragments); 0 (Thrombospondin 1)

L14 ANSWER 8 OF 26 MEDLINE on STN  
AN 1998278601 MEDLINE  
DN PubMed ID: 9618039  
TI Mutant p53 correlates with reduced expression of thrombospondin-1, increased angiogenesis, and metastatic progression in melanoma.  
AU Grant S W; Kyshtoobayeva A S; Kurosaki T; Jakowitz J; Fruehauf J P  
CS Department of Surgery, University of California, Irvine College of Medicine, USA.  
SO Cancer detection and prevention, (1998) 22 (3) 185-94.  
Journal code: 7704778. ISSN: 0361-090X.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199902  
ED Entered STN: 19990316  
Last Updated on STN: 19990316  
Entered Medline: 19990226  
AB On the basis of reports linking mutant p53 (mp53) to decreased expression of the angiogenesis inhibitor thrombospondin-1 (TSP-1) and increased angiogenesis, we compared primary and metastatic melanoma tumor specimens to determine if these factors were associated with metastatic progression. Western blotting, immunohistochemistry (IHC), and image analysis (IA) techniques were employed to evaluate the relationship between p53 status and TSP-1 expression in Zaz and M14 melanoma cell lines, and among p53, TSP-1, and angiogenesis in primary and metastatic melanomas. Zaz cells expressed wild-type p53 (WT p53) and high levels of TSP-1, while the M14 cells expressed mp53 and low TSP-1 levels. Examination of clinical melanoma specimens (N = 99) revealed an incidence of mp53 of 48%. Specimens with WT p53 (N = 46) expressed significantly higher mean levels of TSP-1 (41 +/- 27 vs. 21 +/- 24; p = 0.0004), and lower microvessel counts per 200x field (25 +/- 17 vs. 40 +/- 20; p = 0.0001) than tumors expressing mp53 (N = 42). A significantly higher incidence of mp53 expression was seen in metastatic tumors (64%, 37/58) than in primary tumors (27%, 11/41) (p < 0.0005). Primary tumors specimens had higher levels of TSP-1 (40 +/- 27 vs. 25 +/- 25; p = 0.0054) and lower microvessel counts (26 +/- 18 vs. 39 +/- 20, p = 0.0013) than metastatic tumors. These data suggest that acquisition of mp53, decreased TSP-1, and increased microvessel infiltration may be interrelated and associated with the metastatic phenotype in malignant melanoma.  
CT Blotting, Western  
    \*Genes, p53: GE, genetics  
    Humans  
    Immunohistochemistry  
        Melanoma: BS, blood supply  
        \*Melanoma: GE, genetics  
        \*Melanoma: SC, secondary  
    \*Mutation: GE, genetics  
    \*Neovascularization, Pathologic: GE, genetics

Thrombospondins: AI, antagonists & inhibitors  
\*Thrombospondins: BI, biosynthesis  
Tumor Cells, Cultured  
CN 0 (Thrombospondins)

L14 ANSWER 9 OF 26 MEDLINE on STN  
AN 96049797 MEDLINE  
DN PubMed ID: 8534861  
TI The modulation of thrombospondin and other naturally occurring inhibitors of angiogenesis during tumor progression.  
AU Volpert O V; Stellmach V; Bouck N  
CS Department of Microbiology-Immunology, Northwestern University, Chicago, IL 60611, USA.  
NC RO1 CA27350 (NCI)  
SO Breast cancer research and treatment, (1995) 36 (2) 119-26. Ref: 56  
Journal code: 8111104. ISSN: 0167-6806.  
CY Netherlands  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LA English  
FS Priority Journals  
EM 199602  
ED Entered STN: 19960221  
Last Updated on STN: 19980206  
Entered Medline: 19960207  
AB Fifteen different natural inhibitors of angiogenesis have now been identified that are produced by mammalian cells and are able to block in vivo neovascularization. The majority of these are able to inhibit endothelial cell activities in vitro and all those tested have demonstrated significant antitumor activity. Most normal cells produce inhibitors of neovascularization that must be downregulated before the cells can develop into angiogenic, malignant tumors. In several cases the production of inhibitors ceases when tumor suppressor genes are inactivated. In the BT549 human breast carcinoma cell line, the reintroduction of a wild type p53 tumor suppressor gene resulted in the stimulation of the secretion of an inhibitor of angiogenesis, thrombospondin-1, and as a result the cells lost their angiogenic phenotype and became able to suppress angiogenesis induced by the parental tumor line. These results provide a new example of tumor suppressor gene control of a natural inhibitor of angiogenesis and add support to the concept that thrombospondin loss may play an important role in the development of some human breast cancers.  
CT Animals  
\*Breast Neoplasms: BS, blood supply  
\*Breast Neoplasms: ME, metabolism  
Cell Adhesion Molecules: BI, biosynthesis  
Cell Adhesion Molecules: ME, metabolism  
Disease Progression  
Down-Regulation  
Humans  
\*Membrane Glycoproteins: BI, biosynthesis  
Membrane Glycoproteins: PH, physiology  
\*Neovascularization, Pathologic: ME, metabolism  
Research Support, Non-U.S. Gov't  
Research Support, U.S. Gov't, P.H.S.  
Thrombospondins  
CN 0 (Cell Adhesion Molecules); 0 (Membrane Glycoproteins); 0 (Thrombospondins)

L14 ANSWER 10 OF 26 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
AN 2001:85345 BIOSIS

DN PREV200100085345  
TI Angiogenesis index (AI) is associated with early recurrence in patients presenting with primary breast cancer.  
AU Ellis, R. J. [Reprint author]; Kimler, B. F. [Reprint author]; Fabian, C. J. [Reprint author]; Tawfik, O. [Reprint author]; Mehta, R. S.; Kysthoobayeva, A.; Fruehauf, J. P.  
CS University of Kansas Medical Center, Kansas City, KS, USA  
SO Breast Cancer Research and Treatment, (November, 2000) Vol. 64, No. 1, pp. 101. print.  
Meeting Info.: 23rd Annual San Antonio Breast Cancer Symposium. San antonio, Texas, USA. December 06-09, 2000. Cancer Therapy and Research Center Research Foundation.  
CODEN: BCTR6. ISSN: 0167-6806.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)  
LA English  
ED Entered STN: 14 Feb 2001  
Last Updated on STN: 12 Feb 2002  
CC Immunology - General and methods 34502  
General biology - Symposia, transactions and proceedings 00520  
Biochemistry studies - Proteins, peptides and amino acids 10064  
Biochemistry studies - Sterols and steroids 10067  
Cardiovascular system - Physiology and biochemistry 14504  
Blood - Blood and lymph studies 15002  
Blood - Blood cell studies 15004  
Reproductive system - Physiology and biochemistry 16504  
Reproductive system - Pathology 16506  
Endocrine - General 17002  
Neoplasms - Immunology 24003  
Neoplasms - Pathology, clinical aspects and systemic effects 24004  
Immunology - Immunopathology, tissue immunology 34508  
IT Major Concepts  
Gynecology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences); Methods and Techniques  
IT Parts, Structures, & Systems of Organisms  
blood vessel: circulatory system; breast: reproductive system, histology; lymph node: blood and lymphatics, immune system, histology  
IT Diseases  
primary breast cancer: neoplastic disease, reproductive system disease/female, early recurrence, grade, invasiveness  
Breast Neoplasms (MeSH)  
IT Chemicals & Biochemicals  
CD31: biomarker, expression; estrogen; estrogen receptor: expression; p53: biomarker, expression; progesterone; progesterone receptor: expression; thrombospondin-1 [TSP-1]: biomarker, expression  
IT Methods & Equipment  
angiogenesis index: scoring method  
IT Miscellaneous Descriptors  
age; angiogenesis; blood vessel density; estrogen receptor status; invasive phenotype; lymph node status; progesterone receptor status; survival rate; tumor grade; tumor size; Meeting Abstract; Meeting Poster  
ORGN Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
human: female, patient  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates  
RN 57-83-0 (progesterone)

L14 ANSWER 11 OF 26 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 2000:238815 BIOSIS

DN PREV200000238815

TI Importance of vascular endothelial growth factor (VEGF) and thrombospondin-1 (TSP-1) in melanoma angiogenesis, and independent prognostic significance of microvessel density.

AU Straume, Oddbjorn [Reprint author]; Akslen, Lars A. [Reprint author]

CS Gade Institute, Bergen, Norway

SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 511. print.  
Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 01-05, 2000.  
ISSN: 0197-016X.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 7 Jun 2000  
Last Updated on STN: 5 Jan 2002

CC Neoplasms - General 24002  
Biochemistry studies - General 10060  
Cardiovascular system - General and methods 14501  
General biology - Symposia, transactions and proceedings 00520

IT Major Concepts  
Cardiovascular System (Transport and Circulation); Tumor Biology

IT Parts, Structures, & Systems of Organisms  
microvessels: circulatory system, density

IT Diseases  
melanoma: neoplastic disease  
Melanoma (MeSH)

IT Chemicals & Biochemicals  
Ki-67: expression; p16 protein: expression; p53: expression;  
thrombospondin-1: expression; vascular endothelial growth factor: expression

IT Methods & Equipment  
immunohistochemistry: analytical method; in situ hybridization:  
analytical method

IT Miscellaneous Descriptors  
angiogenesis; disease prognosis; disease survival; tumor stage; Meeting Abstract

ORGN Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name  
human: patient

Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 127464-60-2 (vascular endothelial growth factor)

L14 ANSWER 12 OF 26 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 1998:280331 BIOSIS

DN PREV199800280331

TI p53 and angiogenesis in neoplasia.

AU Gasparini, Giampietro [Reprint author]; Harris, Adrian L.

CS Dep. Oncology, St. Bortolo Hosp., 36100 Vicenze, Italy

SO Klijn, J. G. M. [Editor]. (1997) pp. 115-130. European School of Oncology Scientific Updates, Vol. 1; Prognostic and predictive value of p53. print.  
Publisher: Elsevier Science Publishers B.V., PO Box 211, Sara Burgerhartstraat 25, 1000 AE Amsterdam, The Netherlands; Elsevier Science Publishing Co., Inc., P.O. Box 882, Madison Square Station, New York, New

York 10159-2101, USA.  
ISBN: 0-444-82832-X.

DT Book  
LA Book; (Book Chapter)  
ED Entered STN: 8 Jul 1998  
Last Updated on STN: 8 Jul 1998  
CC Genetics - General 03502  
Biochemistry studies - General 10060  
Metabolism - General metabolism and metabolic pathways 13002  
Cardiovascular system - General and methods 14501  
Neoplasms - General 24002

IT Major Concepts  
Cardiovascular System (Transport and Circulation); Molecular Genetics  
(Biochemistry and Molecular Biophysics); Tumor Biology

IT Diseases  
breast cancer: neoplastic disease, reproductive  
system disease/female  
Breast Neoplasms (MeSH)

IT Chemicals & Biochemicals  
p53: inactivation, mutation, tumor suppressor gene;  
thrombospondin-1

IT Miscellaneous Descriptors  
angiogenesis; Book Chapter

ORGN Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
human: patient  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L14 ANSWER 13 OF 26 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on  
STN

AN 1998:194893 BIOSIS  
DN PREV199800194893

TI Regulation of angiogenesis in carcinoma of the breast, prostate,  
colon, and malignant melanoma by p53 and  
thrombospondin-1 (TSP1).

AU Fruehauf, J. P. [Reprint author]; Mehta, R.; Mechettner, E.; Kurosaki, T.;  
Jackowitz, J.; Grant, S.; Kyshtoobayeva, A.

CS Oncotech Inc., Irvine, CA 92614, USA

SO Proceedings of the American Association for Cancer Research Annual  
Meeting, (March, 1998) Vol. 39, pp. 150. print.  
Meeting Info.: 89th Annual Meeting of the American Association for Cancer  
Research. New Orleans, Louisiana, USA. March 28-April 1, 1998. American  
Association for Cancer Research.  
ISSN: 0197-016X.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English  
ED Entered STN: 4 May 1998  
Last Updated on STN: 4 May 1998  
CC Neoplasms - Biochemistry 24006  
Cardiovascular system - Physiology and biochemistry 14504  
Reproductive system - Pathology 16506  
General biology - Symposia, transactions and proceedings 00520

IT Major Concepts  
Cardiovascular System (Transport and Circulation); Cell Biology; Tumor  
Biology

IT Diseases  
breast carcinoma: neoplastic disease, reproductive system  
disease/female

Breast Neoplasms (MeSH); Carcinoma (MeSH)  
IT Diseases  
colon carcinoma: digestive system disease, neoplastic disease  
Colonic Neoplasms (MeSH); Carcinoma (MeSH)  
IT Diseases  
malignant melanoma: neoplastic disease  
Melanoma (MeSH)  
IT Diseases  
prostate carcinoma: neoplastic disease, reproductive system  
disease/male, urologic disease  
Prostatic Neoplasms (MeSH); Carcinoma (MeSH)  
IT Chemicals & Biochemicals  
p53; thrombospondin-1 [TSP1]  
IT Miscellaneous Descriptors  
angiogenesis regulation; tumor physiology; Meeting Abstract

L14 ANSWER 14 OF 26 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
AN 1998:154913 BIOSIS  
DN PREV199800154913  
TI Thrombospondin-1 in invasive breast cancer and its association with p53 expression, micro vessel density and clinical outcome.  
AU Steward, M. A. [Reprint author]; Rice, A. J.; Roberts, D.; Benson, E. A.; Horgan, K.; Quinn, C. M.  
CS Dep. Surg., Gen. Infirmary at Leeds, Leeds, UK  
SO Journal of Pathology, (1998) Vol. 184, No. SUPPL., pp. 5A. print.  
Meeting Info.: 176th Meeting of the Pathological Society of Great Britain and Ireland. London, England, UK. January 7-9, 1998. Departments of Histopathology and Medical Microbiology, Imperial College School of Medicine at Charing Cross, London.  
CODEN: JPTLAS. ISSN: 0022-3417.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English  
ED Entered STN: 31 Mar 1998  
Last Updated on STN: 31 Mar 1998  
CC Pathology - General 12502  
Microscopy - Histology and histochemistry 01056  
Biochemistry studies - Proteins, peptides and amino acids 10064  
Replication, transcription, translation 10300  
Pathology - Diagnostic 12504  
Metabolism - Proteins, peptides and amino acids 13012  
Cardiovascular system - General and methods 14501  
Reproductive system - General and methods 16501  
Neoplasms - Pathology, clinical aspects and systemic effects 24004  
Neoplasms - Biochemistry 24006  
Neoplasms - Carcinogens and carcinogenesis 24007  
General biology - Symposia, transactions and proceedings 00520  
IT Major Concepts  
Reproductive System (Reproduction); Tumor Biology  
IT Diseases  
breast cancer: neoplastic disease, reproductive system disease/female  
Breast Neoplasms (MeSH)  
IT Diseases  
invasive breast cancer: neoplastic disease, reproductive system disease/female  
Breast Neoplasms (MeSH)  
IT Chemicals & Biochemicals  
p53: expression; thrombospondin-1  
IT Methods & Equipment  
immunohistochemistry: analytical method  
IT Miscellaneous Descriptors

angiogenesis; clinical outcome; micro vessel density; tumor  
grades; Meeting Abstract

ORGN Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
human: female, patient  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L14 ANSWER 15 OF 26 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on  
STN

AN 1997:422735 BIOSIS

DN PREV199799721938

TI Control of inhibitors of angiogenesis by tumor suppressor genes.

AU Bouck, Noel

CS Northwest. Univ. Med. Sch., Chicago, IL, USA

SO FASEB Journal, (1997) Vol. 11, No. 9, pp. A1450.  
Meeting Info.: 17th International Congress of Biochemistry and Molecular  
Biology in conjunction with the Annual Meeting of the American Society for  
Biochemistry and Molecular Biology. San Francisco, California, USA. August  
24-29, 1997.  
CODEN: FAJOEC. ISSN: 0892-6638.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 8 Oct 1997  
Last Updated on STN: 8 Oct 1997

CC General biology - Symposia, transactions and proceedings 00520  
Genetics - Animal 03506  
Biochemistry studies - Proteins, peptides and amino acids 10064  
Biophysics - Membrane phenomena 10508  
Cardiovascular system - Blood vessel pathology 14508  
Respiratory system - Pathology 16006  
Endocrine - General 17002  
Neoplasms - Biochemistry 24006  
Neoplasms - Carcinogens and carcinogenesis 24007

IT Major Concepts  
Biochemistry and Molecular Biophysics; Cardiovascular Medicine (Human  
Medicine, Medical Sciences); Endocrine System (Chemical Coordination  
and Homeostasis); Genetics; Membranes (Cell Biology); Oncology (Human  
Medicine, Medical Sciences); Pulmonary Medicine (Human Medicine,  
Medical Sciences)

IT Miscellaneous Descriptors  
ANGIOGENESIS; BASIC FIBROBLAST GROWTH FACTOR; BFGF; CD36;  
FIBROSARCOMA; LUNG METASTASIS; MELANOMA; MICROVASCULAR CELL;  
MIGRATION; MOLECULAR GENETICS; NEOPLASTIC DISEASE; P53;  
RESPIRATORY SYSTEM DISEASE; THROMBOSPONDIN-1; TUMOR  
BIOLOGY; VASCULAR ENDOTHELIAL GROWTH FACTOR; VEGF

ORGN Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
human  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier  
Muridae 86375  
Super Taxa  
Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
mouse

Taxa Notes

Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

L14 ANSWER 16 OF 26 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 1997:249509 BIOSIS

DN PREV199799548712

TI Regulation of genes associated with angiogenesis, growth, and metastasis by specific p53 point mutations in a murine melanoma cell line.

AU Koura, Aaryan N.; Van Golen, Kenneth; Tsan, Rachel; Radinsky, Robert; Price, Janet E.; Ellis, Lee M. [Reprint author]

CS Dep. Surg. Oncol., Box 106, Univ. Texas M.D. Anderson Cancer Cent., 1515 Holcombe Blvd., Houston, TX 77030, USA

SO Oncology Reports, (1997) Vol. 4, No. 3, pp. 475-479.  
ISSN: 1021-335X.

DT Article

LA English

ED Entered STN: 13 Jun 1997  
Last Updated on STN: 13 Jun 1997

AB K1735 murine melanoma cells transfected with p53 cDNAs bearing specific point mutations are metastatic in nude mice, whereas the parent and control-transfected cells are nonmetastatic. To determine whether p53 gene mutations regulate genes associated with angiogenesis, growth, and metastasis, we examined expression of vascular endothelial growth factor, transforming growth factor-beta, mdm-2, insulin-like growth factor I, IGF-I receptor, epidermal growth factor receptor, c-MET, and thrombospondin 1 in K1735 cells transfected with one of four different mutant p53 cDNAs. Northern blot analysis demonstrated differential upregulation of these genes in cells transfected with different mutant p53 cDNAs. Up-regulation of angiogenesis-, growth-, and metastasis-related genes by mutant p53 may contribute to metastasis formation.

CC Genetics - Animal 03506  
Biochemistry studies - General 10060  
Neoplasms - General 24002

IT Major Concepts  
Biochemistry and Molecular Biophysics; Genetics; Tumor Biology

IT Chemicals & Biochemicals  
INSULIN-LIKE GROWTH FACTOR I

IT Miscellaneous Descriptors  
ANGIOGENESIS; C-MET; EPIDERMAL GROWTH FACTOR RECEPTOR;  
EXPRESSION; GENE REGULATION; GENETICS; INSULIN-LIKE GROWTH FACTOR I;  
INSULIN-LIKE GROWTH FACTOR I RECEPTOR; K1735 CELL LINE; MDM-2;  
METASTASIS; MURINE MELANOMA CELLS; NUDE MOUSE; P53  
DNA; P53 POINT MUTATIONS; THROMBOSPONDIN 1  
; TRANSFORMING GROWTH FACTOR-BETA; TUMOR BIOLOGY; TUMOR GROWTH;  
VASCULAR ENDOTHELIAL GROWTH FACTOR

ORGN Classifier  
Muridae 86375  
Super Taxa  
Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
Muridae  
Taxa Notes  
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 67763-96-6 (INSULIN-LIKE GROWTH FACTOR I)

L14 ANSWER 17 OF 26 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 1997:233070 BIOSIS

DN PREV199799532273

TI P53, thrombospondin-1 (TSP-1),  
angiogenesis (ANG) and androgen receptor (AR) as prognostic  
factors in prostate cancer (PC).  
AU Mehta, R. [Reprint author]; Kyshtoobayeva, A.; Kurosaki, T.; Small, E.;  
Stroop, R.; Fruehauf, J.  
CS Oncotech Inc., Irvine, CA 92614, USA  
SO Proceedings of the American Association for Cancer Research Annual  
Meeting, (1997) Vol. 38, No. 0, pp. 429.  
Meeting Info.: Eighty-eighth Annual Meeting of the American Association  
for Cancer Research. San Diego, California, USA. April 12-16, 1997.  
ISSN: 0197-016X.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English  
ED Entered STN: 2 Jun 1997  
Last Updated on STN: 2 Jun 1997  
CC General biology - Symposia, transactions and proceedings 00520  
Biophysics - Membrane phenomena 10508  
Metabolism - Carbohydrates 13004  
Metabolism - Proteins, peptides and amino acids 13012  
Cardiovascular system - Blood vessel pathology 14508  
Blood - Blood cell studies 15004  
Urinary system - Pathology 15506  
Reproductive system - Pathology 16506  
Neoplasms - Biochemistry 24006  
IT Major Concepts  
Blood and Lymphatics (Transport and Circulation); Cardiovascular  
Medicine (Human Medicine, Medical Sciences); Membranes (Cell Biology);  
Metabolism; Oncology (Human Medicine, Medical Sciences); Reproductive  
System (Reproduction); Urology (Human Medicine, Medical Sciences)  
IT Miscellaneous Descriptors  
ANDROGEN RECEPTOR; ANGIOGENESIS; EXPRESSION; NEOPLASTIC  
DISEASE; PATIENT; PROGNOSTIC MARKER; PROSTATE CANCER  
; P53; REPRODUCTIVE SYSTEM DISEASE/MALE; SURVIVAL;  
THROMBOSPONDIN-1; TUMOR BIOLOGY; UROLOGIC DISEASE  
ORGN Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
human  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates  
L14 ANSWER 18 OF 26 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on  
STN  
AN 1997:231779 BIOSIS  
DN PREV199799530982  
TI Mutant p53, TSP-1, and angiogenesis: An index of  
metastatic risk in breast cancer.  
AU Fruehauf, J. [Reprint author]; Kyshtoobayeva, A.; Yeatman, T.; Coppola,  
D.; Kurosaki, T.; Kim, H.  
CS Oncotech Inc., Irvine, CA 92614, USA  
SO Proceedings of the American Association for Cancer Research Annual  
Meeting, (1997) Vol. 38, No. 0, pp. 234-235.  
Meeting Info.: Eighty-eighth Annual Meeting of the American Association  
for Cancer Research. San Diego, California, USA. April 12-16, 1997.  
ISSN: 0197-016X.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LA English  
ED Entered STN: 2 Jun 1997  
Last Updated on STN: 2 Jun 1997  
CC General biology - Symposia, transactions and proceedings 00520

Cytology - Human 02508  
Genetics - Human 03508  
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062  
Biochemistry studies - Proteins, peptides and amino acids 10064  
Replication, transcription, translation 10300  
Biophysics - Molecular properties and macromolecules 10506  
Anatomy and Histology - Microscopic and ultramicroscopic anatomy 11108  
Pathology - Diagnostic 12504  
Metabolism - Proteins, peptides and amino acids 13012  
Metabolism - Nucleic acids, purines and pyrimidines 13014  
Cardiovascular system - Physiology and biochemistry 14504  
Cardiovascular system - Blood vessel pathology 14508  
Reproductive system - Anatomy 16502  
Reproductive system - Physiology and biochemistry 16504  
Reproductive system - Pathology 16506  
Neoplasms - Diagnostic methods 24001  
Neoplasms - Immunology 24003  
Neoplasms - Biochemistry 24006  
Neoplasms - Carcinogens and carcinogenesis 24007  
Development and Embryology - Morphogenesis 25508  
Immunology - General and methods 34502

IT Major Concepts  
Biochemistry and Molecular Biophysics; Cardiovascular Medicine (Human Medicine, Medical Sciences); Cardiovascular System (Transport and Circulation); Cell Biology; Development; Genetics; Immune System (Chemical Coordination and Homeostasis); Metabolism; Molecular Genetics (Biochemistry and Molecular Biophysics); Morphology; Oncology (Human Medicine, Medical Sciences); Pathology; Reproductive System (Reproduction)

IT Miscellaneous Descriptors  
ANGIOGENESIS; BLOOD VESSEL FORMATION INHIBITOR;  
BREAST CANCER; DIAGNOSTIC METHOD; EXPRESSION; FEMALE;  
GENETIC DISEASE; IMMUNOHISTOCHEMISTRY; IMMUNOLOGIC METHOD; MEDICAL GENETICS; METASTASIS; METASTATIC RISK; MOLECULAR BIOLOGY; MUTANT P53; MUTATION; NEOPLASTIC DISEASE; ONCOLOGY; PATIENT;  
P53 TUMOR SUPPRESSOR GENE; REPRODUCTIVE SYSTEM DISEASE/FEMALE;  
SURVIVAL; THROMBOSPONDIN-1; TSP-1; TUMOR PROGRESSION

ORGN Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
human  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L14 ANSWER 19 OF 26 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
AN 1996:254681 BIOSIS  
DN PREV199698810810  
TI Mutant p53, decreased thrombospondin-1, and angiogenesis may contribute to breast cancer progression.  
AU Parker, R. J. [Reprint author]; Kyshtoobayeva, A. [Reprint author]; Grant, S.; Fruehauf, J. P. [Reprint author]  
CS Oncotech Inc., Irvine, CA 92714, USA  
SO Proceedings of the American Association for Cancer Research Annual Meeting, (1996) Vol. 37, No. 0, pp. 83.  
Meeting Info.: 87th Annual Meeting of the American Association for Cancer Research. Washington, D.C., USA. April 20-24, 1996.  
ISSN: 0197-016X.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LA Conference; (Meeting Poster)  
ED English  
ED Entered STN: 31 May 1996  
Last Updated on STN: 31 May 1996  
CC General biology - Symposia, transactions and proceedings 00520  
Biochemistry studies - Proteins, peptides and amino acids 10064  
Cardiovascular system - Blood vessel pathology 14508  
Blood - Lymphatic tissue and reticuloendothelial system 15008  
Reproductive system - Pathology 16506  
Neoplasms - Pathology, clinical aspects and systemic effects 24004  
Neoplasms - Carcinogens and carcinogenesis 24007  
Development and Embryology - Morphogenesis 25508  
IT Major Concepts  
Blood and Lymphatics (Transport and Circulation); Cardiovascular Medicine (Human Medicine, Medical Sciences); Development; Oncology (Human Medicine, Medical Sciences); Reproductive System (Reproduction)  
IT Miscellaneous Descriptors  
MEETING ABSTRACT; MEETING POSTER; METASTASIS; ONCOGENESIS; TUMOR GROWTH  
ORGN Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
human  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates, Vertebrates  
L14 ANSWER 20 OF 26 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN  
AN 2005467811 EMBASE  
TI Prognostic and predictive molecular markers in DCIS: A review.  
AU Nofech-Mozes S.; Spayne J.; Rakovitch E.; Hanna W.  
CS W. Hanna, Sunnybrook and Women's College Health Sciences Centre, 2075 Bayview Ave., Toronto, Ont. M4N 3M5, Canada. wedad.hanna@sw.ca  
SO Advances in Anatomic Pathology, (2005) Vol. 12, No. 5, pp. 256-264.  
Refs: 117  
ISSN: 1072-4109  
CY United States  
DT Journal; General Review  
FS 005 General Pathology and Pathological Anatomy  
016 Cancer  
029 Clinical Biochemistry  
LA English  
SL English  
ED Entered STN: 20051110  
Last Updated on STN: 20051110  
AB Eighteen percent of all new breast cancers detected on screening mammography are ductal carcinoma in situ (DCIS), a preinvasive lesion that is highly curable. However, some women with DCIS will develop life-threatening invasive breast cancer. Because the determinants of invasive recurrence are unknown, all women with DCIS require the same treatment (usually with surgery and radiation). Therefore, there is a need to identify biologic markers and create a profile that will provide prognostic information that is more accurate than the currently used van Nuys Index to predict invasive recurrence. In the present review, we examined the many biologic markers studied in breast cancer, describe their main biologic role and their expression in DCIS, and review the various studies regarding their ability to serve as prognostic factors in breast cancer with an emphasis on predicting invasive recurrence in patients with DCIS. This review covers established markers, namely, ER, PR and HER2/neu, that are used routinely to make treatment decisions as well as investigative biologic factors involved in cell proliferation, cell cycle regulation, extracellular molecules, factors involved in extracellular matrix

degradation, and angiogenesis. However, controversies exist regarding the value of these prognostic factors, their interrelationship, and their advantages over morphologic evaluation. Copyright .COPYRGT.  
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CT Medical Descriptors:  
\*breast carcinoma: DI, diagnosis  
\*breast carcinoma: ET, etiology  
\*intraductal carcinoma: DI, diagnosis  
\*intraductal carcinoma: ET, etiology  
\*carcinoma in situ: DI, diagnosis  
\*carcinoma in situ: ET, etiology  
breast disease: DI, diagnosis  
breast disease: ET, etiology  
cancer recurrence  
prediction  
cell cycle  
mitogenesis  
    angiogenesis  
extracellular matrix  
breast carcinogenesis  
prognosis  
human  
review  
priority journal  
Drug Descriptors:  
\*estrogen receptor: EC, endogenous compound  
\*progesterone receptor: EC, endogenous compound  
\*epidermal growth factor receptor 2: EC, endogenous compound  
\*mitosin: EC, endogenous compound  
\*biological marker: EC, endogenous compound  
tumor marker: EC, endogenous compound  
Ki 67 antigen: EC, endogenous compound  
telomerase: EC, endogenous compound  
cyclin D1: EC, endogenous compound  
cyclin A: EC, endogenous compound  
    protein p53: EC, endogenous compound  
protein bcl 2: EC, endogenous compound  
protein p21: EC, endogenous compound  
somatomedin binding protein related protein 1: EC, endogenous compound  
cadherin: EC, endogenous compound  
psoriasis: EC, endogenous compound  
urokinase: EC, endogenous compound  
matrix metalloproteinase: EC, endogenous compound  
discoidin: EC, endogenous compound  
discoidin domain receptor: EC, endogenous compound  
CD31 antigen: EC, endogenous compound  
CD34 antigen: EC, endogenous compound  
blood clotting factor 8: EC, endogenous compound  
cyclooxygenase 2: EC, endogenous compound  
    thrombospondin 1: EC, endogenous compound  
messenger RNA  
complementary DNA  
unclassified drug  
RN (epidermal growth factor receptor 2) 137632-09-8; (protein bcl 2)  
219306-68-0; (protein p21) 85306-28-1; (urokinase) 139639-24-0;  
(discoidin) 81669-85-4, 81669-86-5; (blood clotting factor 8) 9001-27-8; (  
thrombospondin 1) 343987-56-4

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AN 2005170453 EMBASE

TI Small interfering RNA for experimental cancer therapy.

AU Tong A.W.; Zhang Y.-A.; Nemunaitis J.

CS A.W. Tong, Mary Crowley Medical Research Center, 3500 Gaston Avenue,

SO Dallas, TX 75246, United States. alext@baylorhealth.edu  
Current Opinion in Molecular Therapeutics, (2005) Vol. 7, No. 2, pp.  
114-124.

CY Refs: 98  
ISSN: 1464-8431 CODEN: CUOTFO

DT United Kingdom  
FS Journal; General Review  
004 Microbiology  
016 Cancer  
022 Human Genetics  
030 Pharmacology  
037 Drug Literature Index  
039 Pharmacy

LA English  
SL English  
ED Entered STN: 20050428  
Last Updated on STN: 20050428

AB RNA interference describes the recently discovered process of sequence-specific, post-transcriptional gene silencing that is initiated by double-stranded RNA molecules known as small interfering RNAs (siRNAs). siRNAs have an acceptable half-life in vitro, a predictable biodistribution profile similar to that of single-stranded antisense oligonucleotides (ASOs), and have repeatedly been more robust than ASO techniques in terms of consistency of transcript knockdown and threshold concentration. Following validation in mammalian cells by Tuschl and co-workers in 2001, synthetic siRNAs have gained wide acceptance as a laboratory tool for target validation. Currently, there is considerable interest in the therapeutic use of siRNA, particularly in areas of infectious disease and cancer. In vitro and in vivo findings demonstrate the efficacy of siRNA knockdown of gene messages that are pivotal for tumor cell growth, metastasis, angiogenesis and chemoresistance, leading to tumor growth suppression. However, siRNA-based cancer therapy faces similar pharmacokinetic limitations to ASO therapy with respect to the extent that siRNA accesses primary and metastatic target cells. The recently identified 'off-target activity' of siRNAs is also of concern. The concept of carrier-restricted delivery of siRNA by conditionally replicative, oncolytic adenoviruses is discussed. Oncolytic adenoviral delivery offers the potential benefits of restricted and renewable siRNA expression within the tumor microenvironment, an additive antitumor outcome through viral oncolysis and siRNA-mediated oncogene silencing, and a proven clinical platform with respect to infectivity and safety.

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CT Medical Descriptors:  
RNA interference  
posttranscriptional gene silencing  
drug half life  
drug distribution  
validation process  
drug efficacy  
tumor growth  
drug targeting  
metastasis  
tumor vascularization  
cancer resistance  
cancer inhibition  
adenovirus vector  
viral gene delivery system  
antineoplastic activity  
oncolytic virus  
oncogene  
drug safety  
virus infectivity  
treatment outcome  
autoimmune hepatitis: DT, drug therapy

breast cancer: DT, drug therapy  
pancreas adenocarcinoma: DT, drug therapy  
drug specificity  
retrovirus vector  
drug potentiation  
drug tolerability  
solid tumor: DT, drug therapy  
dose response  
plasmid vector  
drug design  
viral gene therapy  
glioma: DT, drug therapy  
lentivirus vector  
genetic transduction  
human  
nonhuman  
clinical trial  
review

Drug Descriptors:

\*small interfering RNA: CT, clinical trial  
\*small interfering RNA: CB, drug combination  
\*small interfering RNA: CM, drug comparison  
\*small interfering RNA: DV, drug development  
\*small interfering RNA: IT, drug interaction  
\*small interfering RNA: DT, drug therapy  
\*small interfering RNA: PR, pharmaceutics  
\*small interfering RNA: PK, pharmacokinetics  
\*small interfering RNA: PD, pharmacology  
\*small interfering RNA: IP, intraperitoneal drug administration  
\*small interfering RNA: TU, intratumoral drug administration  
\*small interfering RNA: IV, intravenous drug administration  
\*small interfering RNA: VI, intravitreal drug administration  
antisense oligonucleotide: CT, clinical trial  
antisense oligonucleotide: CM, drug comparison  
antisense oligonucleotide: DO, drug dose  
antisense oligonucleotide: DT, drug therapy  
antisense oligonucleotide: PK, pharmacokinetics  
antisense oligonucleotide: PD, pharmacology  
ribozyme: CT, clinical trial  
ribozyme: CM, drug comparison  
ribozyme: DT, drug therapy  
ribozyme: PD, pharmacology  
ribozyme: SC, subcutaneous drug administration  
liposome: PR, pharmaceutics  
double stranded RNA: DT, drug therapy  
double stranded RNA: PR, pharmaceutics  
double stranded RNA: PD, pharmacology  
double stranded RNA: IP, intraperitoneal drug administration  
double stranded RNA: TU, intratumoral drug administration  
short hairpin RNA: DT, drug therapy  
short hairpin RNA: PR, pharmaceutics  
short hairpin RNA: PD, pharmacology  
short hairpin RNA: TU, intratumoral drug administration  
short hairpin RNA: IV, intravenous drug administration  
gemcitabine: CB, drug combination  
gemcitabine: IT, drug interaction  
gemcitabine: DT, drug therapy  
gemcitabine: PD, pharmacology  
thrombospondin 1: CB, drug combination  
thrombospondin 1: IT, drug interaction  
thrombospondin 1: DT, drug therapy  
thrombospondin 1: PD, pharmacology  
sirna 027: CT, clinical trial  
sirna 027: DT, drug therapy

sirna 027: VI, intravitreal drug administration  
angiozyme: CT, clinical trial  
angiozyme: CM, drug comparison  
angiozyme: DT, drug therapy  
angiozyme: PD, pharmacology  
angiozyme: SC, subcutaneous drug administration  
immunoliposome: PR, pharmaceutics  
protein p53: DT, drug therapy  
protein p53: PR, pharmaceutics  
protein p53: PD, pharmacology  
protein p53: TU, intratumoral drug administration  
adnexin: DT, drug therapy  
adnexin: PR, pharmaceutics  
adnexin: PD, pharmacology  
adnexin: TU, intratumoral drug administration  
ONYX 015: DT, drug therapy  
ONYX 015: PR, pharmaceutics  
ONYX 015: PD, pharmacology  
ONYX 015: IA, intraarterial drug administration  
ONYX 015: TU, intratumoral drug administration  
antineoplastic agent: CT, clinical trial  
antineoplastic agent: CB, drug combination  
antineoplastic agent: CM, drug comparison  
antineoplastic agent: DV, drug development  
antineoplastic agent: DO, drug dose  
antineoplastic agent: IT, drug interaction  
antineoplastic agent: DT, drug therapy  
antineoplastic agent: PR, pharmaceutics  
antineoplastic agent: PK, pharmacokinetics  
antineoplastic agent: PD, pharmacology  
antineoplastic agent: IA, intraarterial drug administration  
antineoplastic agent: IP, intraperitoneal drug administration

CT Drug Descriptors:

antineoplastic agent: TU, intratumoral drug administration  
antineoplastic agent: IV, intravenous drug administration  
antineoplastic agent: VI, intravitreal drug administration  
antineoplastic agent: SC, subcutaneous drug administration  
onyx 411: CB, drug combination  
onyx 411: IT, drug interaction  
onyx 411: DT, drug therapy  
onyx 411: PD, pharmacology  
onyx 411: IV, intravenous drug administration  
onyx 443: DT, drug therapy  
onyx 443: PD, pharmacology  
onyx 443: IV, intravenous drug administration  
ONYX 321: PD, pharmacology  
unclassified drug

RN (gemcitabine) 103882-84-4; (thrombospondin 1)  
343987-56-4

CN (1) Sirna 027; (2) Ingn 201

CO (1) Sirna therapeutics; (2) Introgen

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AN 2004350415 EMBASE

TI Gene-based therapy in prostate cancer.

AU Foley R.; Lawler M.; Hollywood D.

CS Prof. D. Hollywood, Department of Haematology/Oncology, Institute of Molecular Medicine, St. James' Hospital/Trinity College, Dublin 8, Ireland. dhlywood@tcd.ie

SO Lancet Oncology, (1 Aug 2004) Vol. 5, No. 8, pp. 469-479.

Refs: 75

ISSN: 1470-2045 CODEN: LOANBN

PUI S 1470-2045(04)01525-6

CY United States  
DT Journal; General Review  
FS 016 Cancer  
022 Human Genetics  
028 Urology and Nephrology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
039 Pharmacy  
LA English  
SL English  
ED Entered STN: 20040902  
Last Updated on STN: 20040902  
AB Prostate cancer is one of the commonest causes of illness and death from cancer. Radical prostatectomy, radiotherapy, and hormonal therapy are the main conventional treatments. However, gene therapy is emerging as a promising adjuvant to conventional strategies, and several clinical trials are in progress. Here, we outline several approaches to gene therapy for prostate cancer that have been investigated. Methods of gene delivery are described, particularly those that have commonly been used in research on prostate cancer. We discuss efforts to achieve tissue-specific gene delivery, focusing on the use of tissue-specific gene promoters. Finally, the present use of gene therapy for prostate cancer is evaluated. The ability to deliver gene-therapy vectors directly to prostate tissue, and to regulate gene expression in a tissue-specific manner, offers promise for the use of gene therapy in prostate cancer.  
CT Medical Descriptors:  
\*gene therapy  
\*prostate cancer: DT, drug therapy  
\*prostate cancer: PC, prevention  
\*prostate cancer: RT, radiotherapy  
\*prostate cancer: SU, surgery  
morbidity  
cause of death  
cancer mortality  
prostatectomy  
cancer radiotherapy  
cancer hormone therapy  
cancer adjuvant therapy  
viral gene delivery system  
nonviral gene delivery system  
cancer research  
tissue specificity  
gene expression regulation  
drug mechanism  
suicide gene therapy  
promoter region  
cancer immunotherapy  
thrombocytopenia: SI, side effect  
lymphocytopenia: SI, side effect  
human  
nonhuman  
clinical trial  
review  
priority journal  
Drug Descriptors:  
\*antineoplastic agent: AE, adverse drug reaction  
\*antineoplastic agent: CT, clinical trial  
\*antineoplastic agent: CB, drug combination  
\*antineoplastic agent: DT, drug therapy  
\*antineoplastic agent: PR, pharmaceutics  
\*antineoplastic agent: PD, pharmacology  
\*antineoplastic agent: DL, intradermal drug administration

\*antineoplastic agent: IM, intramuscular drug administration  
\*antineoplastic agent: IV, intravenous drug administration  
\*antineoplastic agent: SC, subcutaneous drug administration  
antisense oligonucleotide: CT, clinical trial  
antisense oligonucleotide: DT, drug therapy  
antisense oligonucleotide: TO, drug toxicity  
antisense oligonucleotide: PR, pharmaceutics  
antisense oligonucleotide: PD, pharmacology  
antisense oligonucleotide: IV, intravenous drug administration  
oligonucleotide: PD, pharmacology  
small interfering RNA: PD, pharmacology  
double stranded DNA: PD, pharmacology  
thymidine kinase: AE, adverse drug reaction  
thymidine kinase: CT, clinical trial  
thymidine kinase: CB, drug combination  
thymidine kinase: DT, drug therapy  
thymidine kinase: PR, pharmaceutics  
thymidine kinase: PD, pharmacology  
ganciclovir: CT, clinical trial  
ganciclovir: CB, drug combination  
ganciclovir: DT, drug therapy  
ganciclovir: PR, pharmaceutics  
ganciclovir: PD, pharmacology  
tumor suppressor protein: AE, adverse drug reaction  
tumor suppressor protein: CT, clinical trial  
tumor suppressor protein: DT, drug therapy  
tumor suppressor protein: PR, pharmaceutics  
tumor suppressor protein: PD, pharmacology  
tumor suppressor protein: TU, intratumoral drug administration  
protein p53: DT, drug therapy  
protein p53: PR, pharmaceutics  
protein p53: PD, pharmacology  
protein Bax: PR, pharmaceutics  
protein Bax: PD, pharmacology  
angiogenesis inhibitor: DT, drug therapy  
angiogenesis inhibitor: PR, pharmaceutics  
angiogenesis inhibitor: PD, pharmacology  
thrombospondin 1: DT, drug therapy  
thrombospondin 1: PR, pharmaceutics  
thrombospondin 1: PD, pharmacology  
cytokine: DT, drug therapy  
cytokine: PR, pharmaceutics  
cytokine: PD, pharmacology  
interleukin 2: AE, adverse drug reaction  
interleukin 2: CT, clinical trial  
interleukin 2: DT, drug therapy  
interleukin 2: PR, pharmaceutics  
interleukin 2: PD, pharmacology  
interleukin 2: TU, intratumoral drug administration  
tumor antigen: DT, drug therapy  
tumor antigen: PR, pharmaceutics  
tumor antigen: PD, pharmacology  
tumor antigen: DL, intradermal drug administration  
tumor antigen: IM, intramuscular drug administration  
tumor antigen: SC, subcutaneous drug administration  
prostate specific antigen: AE, adverse drug reaction  
prostate specific antigen: CT, clinical trial  
prostate specific antigen: DT, drug therapy  
prostate specific antigen: PR, pharmaceutics  
prostate specific antigen: PD, pharmacology  
prostate specific antigen: DL, intradermal drug administration  
prostate specific antigen: IM, intramuscular drug administration  
prostate specific antigen: SC, subcutaneous drug administration  
cytosine deaminase: AE, adverse drug reaction

cytosine deaminase: CT, clinical trial  
cytosine deaminase: CB, drug combination  
cytosine deaminase: DT, drug therapy  
cytosine deaminase: PR, pharmaceutics  
cytosine deaminase: PD, pharmacology  
flucytosine: CB, drug combination  
flucytosine: PR, pharmaceutics  
flucytosine: PD, pharmacology  
valaciclovir: CT, clinical trial  
valaciclovir: CB, drug combination  
valaciclovir: DT, drug therapy  
valaciclovir: PR, pharmaceutics  
valaciclovir: PD, pharmacology  
caspase 9: PR, pharmaceutics  
caspase 9: PD, pharmacology  
diphtheria toxin: DT, drug therapy  
diphtheria toxin: EC, endogenous compound

CT Drug Descriptors:  
diphtheria toxin: PR, pharmaceutics  
diphtheria toxin: PD, pharmacology  
granulocyte macrophage colony stimulating factor: CT, clinical trial  
granulocyte macrophage colony stimulating factor: DT, drug therapy  
granulocyte macrophage colony stimulating factor: PR, pharmaceutics  
granulocyte macrophage colony stimulating factor: PD, pharmacology  
granulocyte macrophage colony stimulating factor: DL, intradermal drug administration  
transforming growth factor beta receptor: DT, drug therapy  
transforming growth factor beta receptor: PD, pharmacology  
mutant protein: DT, drug therapy  
mutant protein: PD, pharmacology  
docetaxel: DT, drug therapy  
docetaxel: TO, drug toxicity  
probasin: DT, drug therapy  
protein bcl 2: DT, drug therapy  
kallikrein: DT, drug therapy  
gamma glutamyl hydrolase: DT, drug therapy  
unindexed drug

RN (thymidine kinase) 9002-06-6, 9086-73-1; (ganciclovir) 82410-32-0; (thrombospondin 1) 343987-56-4; (interleukin 2) 85898-30-2; (cytosine deaminase) 9025-05-2; (flucytosine) 2022-85-7; (valaciclovir) 124832-26-4; (caspase 9) 180189-96-2; (docetaxel) 114977-28-5; (protein bcl 2) 219306-68-0; (kallikrein) 8006-48-2, 9001-01-8; (gamma glutamyl hydrolase) 55326-32-4, 9074-87-7

L14 ANSWER 23 OF 26 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN  
AN 2001374392 EMBASE  
TI Review: Molecular pathology of cyclooxygenase-2 in cancer-induced angiogenesis.  
AU Fosslien E.  
CS Dr. E. Fosslien, Department of Pathology (M/C 847), College of Medicine, University of Illinois at Chicago, 1819 West Polk Street, Chicago, IL 60612, United States. efossli@uic.edu  
SO Annals of Clinical and Laboratory Science, (2001) Vol. 31, No. 4, pp. 325-348.  
Refs: 169  
ISSN: 0091-7370 CODEN: ACLSCP  
CY United States  
DT Journal; General Review  
FS 005 General Pathology and Pathological Anatomy  
016 Cancer  
029 Clinical Biochemistry  
030 Pharmacology  
037 Drug Literature Index

LA English  
SL English  
ED Entered STN: 20011108  
Last Updated on STN: 20011108  
AB Cancer-induced angiogenesis is the result of increased expression of angiogenic factors, or decreased expression of anti-angiogenic factors, or a combination of both events. For instance, in colon cancer, the malignant cells, the stromal fibroblasts, and the endothelial cells all exhibit strong staining for cyclooxygenase-2 (COX-2), the rate-controlling enzyme in prostaglandin (PG) synthesis. In various cancer tissues, vascular endothelial growth factor (VEGF) and transforming growth factor  $\beta$  (TGF-  $\beta$ ) co-localize with COX-2. Strong COX-2 and VEGF expression is highly correlated with increased tumor microvascular density (MCD); new vessels proliferate in areas of the tumor that express COX-2. Moreover, high MVD is a predictor of poor prognosis in breast and cervical cancers. COX-2 and VEGF expression are elevated in breast and prostate cancer tissues and their cell-lines. In vitro, PGE2 induces VEGF. Supernatants of cultured cells from breast, prostate, and squamous cell cancers contain angiogenic proteins such as COX-2 and VEGF that induce in vitro angiogenesis. A selective COX-2 inhibitor, NS-398, restores tumor cell apoptosis, reduces microvascular density, and reduces tumor growth of PC-3 prostate carcinoma cells xenografted into nude mice. The COX-2 produced by a malignant tumor and COX-2 produced by the surrounding host tissue both contribute to new vessel formation, which explains how selective COX-2 inhibition reduces tumor growth where the tumor COX-2 gene has been silenced by methylation.  
CT Medical Descriptors:  
    \*angiogenesis  
    \*tumor vascularization  
    molecular biology  
    microvascularization  
    stroma cell  
    fibroblast  
    endothelium cell  
    prostaglandin synthesis  
    colon cancer: ET, etiology  
        breast cancer: ET, etiology  
        prostate cancer: ET, etiology  
    uterine cervix cancer: ET, etiology  
    squamous cell carcinoma: ET, etiology  
    in vitro study  
    apoptosis  
    cancer inhibition  
    carcinogenesis  
    antineoplastic activity  
    human  
    nonhuman  
    review  
    priority journal  
Drug Descriptors:  
    \*cyclooxygenase 2: EC, endogenous compound  
    vasculotropin: EC, endogenous compound  
    transforming growth factor beta: EC, endogenous compound  
    n (2 cyclohexyloxy 4 nitrophenyl)methanesulfonamide: PD, pharmacology  
    celecoxib: PD, pharmacology  
    rofecoxib: PD, pharmacology  
    nonsteroid antiinflammatory agent: PD, pharmacology  
        protein p53: EC, endogenous compound  
    prostaglandin E2: EC, endogenous compound  
    nitric oxide synthase: EC, endogenous compound  
    endoglin: EC, endogenous compound  
    4 (4 cyclohexyl 2 methyl 5 oxazolyl) 2 fluorobenzenesulfonamide: PD, pharmacology

haptoglobin: EC, endogenous compound  
thrombospondin 1: EC, endogenous compound  
angiostatin: EC, endogenous compound  
metalloproteinase inhibitor: EC, endogenous compound  
CD31 antigen: EC, endogenous compound  
RN (vasculotropin) 127464-60-2; (n (2 cyclohexyloxy 4 nitrophenyl)methanesulfonamide) 123653-11-2; (celecoxib) 169590-42-5; (rofecoxib) 162011-90-7, 186912-82-3; (prostaglandin E2) 363-24-6; (nitric oxide synthase) 125978-95-2; (4 (4 cyclohexyl 2 methyl 5 oxazolyl) 2 fluorobenzenesulfonamide) 180200-68-4; (haptoglobin) 9087-69-8; (angiostatin) 172642-30-7, 86090-08-6  
CN Ns 398; Jte 522

L14 ANSWER 24 OF 26 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN  
AN 2001087714 EMBASE  
TI Expression of thrombospondin-1 in pancreatic carcinoma: Correlation with microvessel density.  
AU Kasper H.U.; Ebert M.; Malfertheiner P.; Roessner A.; Kirkpatrick C.J.; Wolf H.K.  
CS H.U. Kasper, Department of Pathology, Otto-von-Guericke University, Leipziger Strasse 44, 39112 Magdeburg, Germany. hukasper@hotmail.com  
SO Virchows Archiv, (2001) Vol. 438, No. 2, pp. 116-120.  
Refs: 38  
ISSN: 0945-6317 CODEN: VARCEM  
CY Germany  
DT Journal; Article  
FS 016 Cancer  
048 Gastroenterology  
LA English  
SL English  
ED Entered STN: 20010406  
Last Updated on STN: 20010406  
AB Thrombospondin-1 (TSP-1) is a multifunctional platelet and extracellular matrix protein that is involved in angiogenesis. Under certain pathological conditions, e.g., malignant tumors, high concentrations of TSP-1 work as an angiogenic agonist. Here we examined 98 pancreatic carcinomas with respect to TSP-1 immunoreactivity and its correlation to intratumoral microvessel density (MVD), a representation of the overall degree of angiogenesis in carcinomas. Northern blot analysis for TSP-1 mRNA was performed in seven additional cases. Eighty-seven tumors showed strong TSP-1 immunoreactivity, nine carcinomas were only weakly positive, and two lesions were negative for TSP-1. TSP-1 immunoreactivity was detected in the extracellular matrix, mostly at the invasion front of the tumor. Using Northern blot analysis, we observed high levels of TSP-1 mRNA in three out of seven pancreatic carcinomas. The mean MVD in pancreatic carcinoma was 38.8 vessels per mm<sup>2</sup>. Tumors with a high expression of TSP-1 showed a higher MVD and the correlation between TSP-1 immunoreactivity and microvessel density was highly significant ( $P=0.003$ ). As a modulator of angiogenesis, TSP-1 is strongly expressed in most pancreatic adenocarcinomas and is likely to contribute to the extensive neovascularization and spread of this highly aggressive tumor.  
CT Medical Descriptors:  
\*pancreas cancer: DI, diagnosis  
\*angiogenesis  
\*gene expression  
Northern blotting  
immunoreactivity  
extracellular matrix  
neovascularization (pathology)  
thrombocyte  
prognosis  
endometrium cancer: DI, diagnosis

breast cancer: DI, diagnosis  
ovary cancer: DI, diagnosis  
colon cancer: DI, diagnosis  
lung adenocarcinoma: DI, diagnosis  
tumor suppressor gene  
human  
major clinical study  
human tissue  
human cell  
article  
priority journal  
Drug Descriptors:  
    \*thrombospondin 1  
messenger RNA  
disulfide  
    protein p53  
protein p16  
RN (disulfide) 16734-12-6

L14 ANSWER 25 OF 26 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN  
AN 1998333116 EMBASE  
TI Gene therapy with p53 and a fragment of thrombospondin I inhibits human breast cancer in vivo.  
AU Xu M.; Kumar D.; Stass S.A.; Mixson A.J.  
CS A.J. Mixson, Department of Pathology, University of Maryland, Building MSTF, 10 S. Pine Street, Baltimore, MD 21201, United States  
SO Molecular Genetics and Metabolism, (1998) Vol. 63, No. 2, pp. 103-109.  
Refs: 24  
ISSN: 1096-7192 CODEN: MGMEFF  
CY United States  
DT Journal; Article  
FS 016 Cancer  
022 Human Genetics  
030 Pharmacology  
037 Drug Literature Index  
LA English  
SL English  
ED Entered STN: 19981028  
Last Updated on STN: 19981028  
AB We recently reported that a p53 encoding plasmid (BAP-p53) complexed to liposomes administered intravenously markedly attenuates the growth of a malignant human breast tumor. We now have found that systemically delivered liposomes complexed to a plasmid expressing an established antiangiogenic peptide of thrombospondin I (BAP-TSPf) decreased the growth of MDA-MB-435 tumors compared to controls in nude mice. Compared to BAP-p53, the BAP-TSPf group had a similar antitumor efficacy. More importantly, liposomes complexed with BAP-TSPf and BAP-p53 synergistically decreased the growth of MDA-MB-435 tumors when compared to either BAP-p53 or BAP-TSPf alone. Furthermore, we also determined that the combination therapy of p53 and TSPf inhibited endothelial cells in vitro more than either p53 or TSPf alone. There was also a significant decrease of the blood vessel density in the combination p53 and TSPf treatment group compared to the control groups. These results suggest that liposomes complexed to a tumor suppressor and antiangiogenic genes may be effective in treating metastatic tumors.  
CT Medical Descriptors:  
    \*gene therapy  
    \*breast cancer: TH, therapy  
plasmid  
antineoplastic activity  
tumor growth  
    angiogenesis

endothelium cell  
tumor suppressor gene  
metastasis  
nonhuman  
mouse  
animal model  
controlled study  
animal tissue  
article  
priority journal  
Drug Descriptors:  
\*liposome: PD, pharmacology  
\*protein p53: PD, pharmacology  
\*thrombospondin 1: PD, pharmacology

L14 ANSWER 26 OF 26 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN  
AN 97352894 EMBASE  
DN 1997352894  
TI Evidence of a dominant transcriptional pathway which regulates an undifferentiated and complete metastatic phenotype.  
AU Barsky S.H.; Sternlicht M.D.; Safarians S.; Nguyen M.; Chin K.; Stewart S.D.; Hiti A.L.; Gray J.W.  
CS S.H. Barsky, Department of Pathology, University of California, Los Angeles School of Medicine, Los Angeles, CA 90024, United States  
SO Oncogene, (1997) Vol. 15, No. 17, pp. 2077-2091.  
Refs: 58  
ISSN: 0950-9232 CODEN: ONCNES  
CY United Kingdom  
DT Journal; Article  
FS 005 General Pathology and Pathological Anatomy  
013 Dermatology and Venereology  
016 Cancer  
022 Human Genetics  
LA English  
SL English  
ED Entered STN: 971204  
Last Updated on STN: 971204  
AB The highly metastatic amelanotic C8161 human melanoma line was found to exhibit complete dominance of its undifferentiated and metastatic phenotype in multiple somatic cell hybridization studies designed to bypass the presence of potential tumor suppressor genes. In a three armed approach involving somatic cell fusions of C8161 with recipient lines of greater differentiation, different lineage, and different tumorigenicity status, the metastatic and undifferentiated phenotype of C8161 was promiscuously dominant. In somatic cell hybrids produced between the C8161 and a group of non-metastatic human melanoma lines which exhibited melanocyte differentiation markers including S100, HMB-45, NKI/C3, aC3, and melanin, the fusions were uniformly metastatic and undifferentiated. In somatic cell hybrids of C8161 and MCF-7 the fusions exhibited an estrogen independent and unresponsive, estrogen receptor (ER) negative, and highly metastatic phenotype. In fusions between C8161 and HMS-1, an immortalized 'benign' human myoepithelial line which produced an abundant extracellular matrix (ECM) and high levels of protease and angiogenic inhibitors including maspin, tissue inhibitor of metalloproteinase-1 (TIMP-1),  $\alpha$ 1-antitrypsin ( $\alpha$ 1-AT), protease nexin II (PN-II), thrombospondin-1 and soluble basic fibroblast growth factor (bFGF) receptors, the hybrids showed complete absence of matrix, absent maspin expression, markedly decreased protease inhibitor and angiogenic inhibitor production, high levels of proteases and angiogenic factors, and a highly metastatic phenotype. In our somatic cell fusions, the human-human hybrids represented true and complete fusions and not hybrid clones selected for by loss of dominant-acting growth suppressor genes. This finding was supported by detailed

comparative genomic hybridization (CGH) studies, Q-banding karyotype analysis, and autofusions of representative clones. The purposeful creation of inherently unstable human-murine fusions between C8161 and B16-F1 where loss of putative suppressor loci would be expected, resulted in fusions exhibiting decreased growth and non-metastatic behavior with progressive chromosomal loss. Neither p53, nm23, DNA methyltransferase, activated ras, fibroblast growth factor-4 (FGF-4), or epidermal growth factor receptor (EGFR) mediated the acquisition of the metastatic or undifferentiated phenotype within the C8161-human fusions. These studies are the first studies ever to successfully transfer the complete metastatic phenotype by somatic cell fusion and support the presence of a new high level regulatory pathway(s) involving dominant trans-acting factors which act pleiotropically to regulate an undifferentiated and highly metastatic phenotype.

CT

Medical Descriptors:

- \*metastasis
- \*transcription regulation
- animal cell
- article
- cell clone
- cell differentiation
- chromosome loss
- controlled study
- extracellular matrix
- gene locus
- genetic transcription
- human
- human cell
- hybrid cell
- karyotyping
- melanocyte
  - melanoma
- mouse
- nonhuman
- phenotype
- priority journal
- somatic cell
- tumor suppressor gene

Drug Descriptors:

- alpha 1 antitrypsin
  - angiogenesis inhibitor
- basic fibroblast growth factor
- dna methyltransferase: EC, endogenous compound
- epidermal growth factor receptor: EC, endogenous compound
- estrogen
- estrogen receptor
- fibroblast growth factor 4: EC, endogenous compound
- fibroblast growth factor receptor
- protease nexin
  - protein p53: EC, endogenous compound
- proteinase inhibitor
- ras protein: EC, endogenous compound
- thrombospondin
- tissue inhibitor of metalloproteinase
- trans acting factor: EC, endogenous compound
  - (alpha 1 antitrypsin) 9041-92-3; (basic fibroblast growth factor) 106096-93-9; (dna methyltransferase) 9037-42-7; (proteinase inhibitor) 37205-61-1; (tissue inhibitor of metalloproteinase) 97837-28-0

RN